

Notice of Allowability

Application No.

10/690,196

Examiner

Yelena G. Gakh, Ph.D.

Applicant(s)

GARDELLA ET AL.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 10/06/04.
2. ☒ The allowed claim(s) is/are 1-5, 7-12, 18 and 19.
3. ☐ The drawings filed on _____ are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 6. ☒ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☒ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____

EXAMINER'S AMENDMENT

1. In the specification, page 1, line 8, after "2003" insert -- now US Patent No. 6,670,190 --

Allowable Subject Matter

2. **Claims 1-5, 7-12 and 18-19** are allowed. The new numbering of claims is 1 through 13.

The following is an examiner's statement of reasons for allowance: the following is the closest prior art:

Davies et al. (Polymers for Advanced Technologies, 1992) disclose "probing the surface chemical structure of some novel poly(ortho esters) prepared with N-methyl- and N-phenyl-ethanolamine by time-of-flight secondary ion mass spectrometry (ToF-SIMS)": "The surface chemical structures of a series of novel poly(ortho ester) homopolymer and copolymer films (I) prepared using N-methyl- and N-phenyl-ethanolamine have been investigated using a time-of-flight secondary-ion mass spectrometry (ToF-SIMS). Systematic fragmentation patterns were observed within the ToF-SIMS spectra up to $m/z = 1600$, which were readily interpreted in terms of the polymer structures. Cations were detected which could be assigned to structures arising from the diols, the ortho ester species and diads, triads etc. of the monomer, from both the homopolymer and the random portion of the copolymer chains. The analysis of the proposed ion structures suggested two major mechanisms of fragmentation based on the cleavage of the ortho ester bonds involving either the exocyclic or the endocyclic alkoxy group. The ToF-SIMS peak area ratios for ions diagnostic of the diols and the ortho ester species reflected the bulk copolymer composition in a semi-quantitative fashion. The observation of such relationships for high-mass cations (up to $m/z = 500$) is particularly noteworthy and has not been reported previously. These studies allow a dramatic insight into the surface chemical structure of these poly(ortho esters)--information which has formed the foundation of current investigations on the mechanisms of the acid-catalyzed surface degradation of these polymers". However, Davies

does not teach determination of *reaction kinetics* of surface degradation of the biodegradable polymers.

Short et al. (Vacuum, 1993) teach "TOF SIMS in polymer surface studies" (Title): "A review with 61 references describing advances made in the study of polymer surfaces at Sheffield University between 1988 and 1993. Over this period, we have taken advantage of the increased surface sensitivity, extended mass range, and imaging capability of Time-of-Flight Secondary Ion Mass Spectrometry (TOF SIMS) to investigate the surfaces of 'as-received', degraded, and modified polymers, as well as organic surface coatings prepared by plasma polymerization. Secondary ion mass spectrometry in polymer surface studies, surface structure of polymer blends, surface photo-oxidation of polystyrene (PS) and photostabilized PS, monitoring the effects of plasma surface treatment by TOF SIMS, and plasma polymer structure are reviewed and discussed. A brief overview of the developments in SIMS technology and experimental methodology that now allow its routine use in polymer surface studies is also presented" (Abstract). Changes of ToF-SIMS spectra in time were recorded to demonstrate "the effect of continuous exposure to UV radiation" of polystyrene on silver. However, Short does not teach determination of reaction kinetics of surface degradation of a biodegradable polymer by ToF SIMS by calculating the degree of polymerization from the molecular weight distribution changing in time followed by calculating the rate of surface degradation of the biopolymer.

Lhoest et al. (Nuclear Instruments & Methods in Physics Research, 1995) disclose "PMMA surface modification under keV and MeV ion bombardment in relation to mammalian cell adhesion" (Title): "Spin casted poly(Methacrylate) (PMMA) films were submitted to Ga⁺ (15 keV), Xe⁺ (4 keV) and He⁺ (1 MeV) ion bombardments with fluences varying between 10⁺¹² and 10⁺¹⁶ ions/cm². The surface modifications were studied by time-of-flight secondary ion mass spectrometry (ToF-SIMS) and XPS. The evolution of ToF-SIMS peaks characteristic of the polymer and of the degradation were followed as a function of the ion fluence. Surface deoxygenation and loss of the methacrylate pendent group were observed. These results are discussed regarding the kind of energy deposition mode (electronic and nuclear). The XPS results confirmed the surface deoxygenation. Finally, the influence of the ion beam modifications on the adhesion of mammalian cells were investigated. For this purpose, the samples were reconditioned by a solution containing both a protein and a surfactant prior to

inoculation with human epithelial cells in a serum free nutritive medium. The results showed a preferential cell adhesion in the bombarded areas" (Abstract). Lhoest does not teach or fairly suggest kinetic measurements of surface degradation of a biodegradable polymer by calculating the degree of polymerization from the molecular weight distribution changing in time followed by calculating the rate of surface degradation of the biopolymer.

Weidner et al. (Rapid Comm. Mass Spectrom., 1996) teach "plasmaoxidative and chemical degradation of poly(ethylene terephthalate) studied by matrix-assisted laser desorption/ionization mass spectrometry" (Title). "A model system of linear ethylene glycol-terminated poly(ethylene terephthalate) oligomers of the general formula $H-[GT]_n-G$ (where G is an ethylene glycol unit and T represents a terephthalic acid unit) was synthesized and exposed to an oxygen plasma. The degradation of the oligomers was investigated by matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS). The results were compared to a chemical degradation of commercial poly(ethylene terephthalate) which had been exposed to an aqueous solution of natural chalk for many years. In both cases an ester scission process was found which generates terephthalic acid-terminated oligomers ($H-[GT]_m-OH$) and decomposes linear ethylene glycol-terminated oligomers ($H-[GT]_m-G$). The scission of the ester bonds during the chemical treatment additionally leads to the formation of $T-[GT]_m-OH$ -like oligomers and to a strong decrease of the number of cyclic oligomers ($[GT]_m$). Furthermore during the plasma treatment an additional formation of $[GT]_m-G$ like cyclic oligomers was observed" (Abstract). Weiner does not teach determination of reaction kinetics of surface degradation of a biodegradable polymer by ToF SIMS.

Saito et al. (Applied Surface Science, 1999) teach "TOF-SIMS analysis of chemical state changes in cresol-novolak photoresist surface caused by O_2 plasma downstream": "The chemical state changes on cresol-novolak photoresist surfaces caused by O_2 plasma exposure were investigated using time-of-flight secondary ion mass spectrometry (TOF-SIMS). TOF-SIMS spectra were measured at the surface of the photoresist samples which were exposed to the O_2 plasma downstream for various exposure times and the spectral intensity changes of characteristic secondary ion species with respect to O_2 plasma conditions were quantitatively evaluated. Oxidation and decomposition of the polymer were observed from analysis of the changes in the peaks originating from the chemical structure of the polymer, both in positive and

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negative mass spectra. It was clarified that oxidation and vaporization attain a balance within a thin altered layer. In addition, depletion of photosensitive additive at the surface was confirmed and the usefulness of TOF-SIMS for predicting the reaction occurring on photoresist surfaces was successfully demonstrated" (Abstract). However, Saito does not teach determination of reaction kinetics of surface degradation of a biodegradable polymer by calculating the degree of polymerization from the molecular weight distribution changing in time followed by calculating the rate of surface degradation of the biopolymer.

Léonard et al. Fresenius J. Anal. Chem., September 1999) disclose "characterization of biomaterials using ToF-SIMS": "in the field of biomaterials and biological compounds, ToF-SIMS has exhibited large interest due to high surface sensitivity, an information depth limited to the top-surface and molecular imaging capabilities. Selected examples given in this review concern recent applications like characterization of engineered heterogeneous bioactive surfaces (including biosensors), combinatorial synthesis of peptides, molecular imaging of cells and quantification of biomolecules in real biological samples. These examples illustrate advantages and possible limitations of ToF-SIMS in this research field" (Abstract).

Chen et al. (Macromolecules, 1999) teaching "Time-of-Flight Secondary Ion Mass Spectrometry studies of *in vitro* hydrolytic degradation of biodegradable polymers" (Title) and *Chen et al. (Macromolecules, 2000)* teaching "Time-of-Flight Secondary Ion Mass spectrometry studies of hydrolytic degradation kinetics at the surfaced of poly(glycolic acid)" are not the prior art of the instant application with the priority date of 10/06/1999.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Drawings

3. New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because they contain informalities indicated in the Notice of Draftsman for the parent

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case. Applicant is advised to employ the services of a competent patent draftsman outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Yelena G. Gakh
10/22/04

